HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

TEST PLAN
FOR
3,3' Dichlorobenzidine Dihydrochloride
(CAS NO.: 612-83-9)

PREPARED BY:
COLOR PIGMENT MANUFACTURERS ASSOCIATION, INC.

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OVERVIEW

The Color Pigment Manufacturers Association, Inc. ("CPMA") and its member companies hereby submits for review and public comment the following test plan for 3,3' Dichlorobenzidine dihydrochloride ("DCB") Chemical Abstract Service ("CAS") No. 612839 under the Environmental Protection Agency's ("EPA") High Production Volume (HPV) Challenge Program. It is the intent of the CPMA and its member companies to use existing data, and predictive computer models to adequately fulfill the Screening Information Data Set ("SIDS") for the various physicochemical, environmental fate, ecotoxicity, and human health effects endpoints.

The parent compound Dichlorobenzidine is a white crystalline solid. The dihydrochloride DCB salt, the major form in actual use, is a stable, grey-to-purple crystalline solid that does not evaporate. This chemical is used as a closed system intermediate in the manufacture of organic color pigments. Due to its reactive properties and potential health concerns, DCB is used in weighted two part reactions in which the coupling agents are added in excess to completely react all DCB used in pigment production reactions. This prevents residual DCB from being present in the finished color pigment products and prevents further exposure to DCB. DCB is strictly regulated as a workplace hazard under existing Occupational Safety and Health Administration regulations. There is no exposure to DCB permitted in the workplace. At this time, there is no DCB manufactured in the United States. A more detailed characterization of DCB is available from the U.S. Agency for Toxic Substances and Disease Registry, Toxicological Profile for DCB. Due to the extensive database of information available on DCB, its limited closed system use in the manufacture of pigments, its regulation as a work place hazard with no exposure limit and the fact that DCB is no longer manufactured in the United States, no further testing of DCB is planned. The analog DCB compounds, free-dichlorobenzidine CAS No. 91-94-1 and dichlorobenzidine Sulfate, CAS No. 74332-73-3 are anticipated to exhibit characteristics similar to DCB dihydrochloride, the primary form of the chemical used in commerce and described in this test plan.

TEST PLAN SUMMARY

CAS No.5468757	Information	OECD Study	Other	Estimation	GLP	Acceptable	New Testing Req.
STUDY	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL DATA							
Melting Point	Y	-	Y	N	N	Y	N
Boiling Point	Y	-	Y-	N	N	Y	N
Vapor Pressure	Y	-	Y	N	N	Y	N
Partition Coefficient	Y	-	Y	N	N	Y	N
Water Solubility	Y	-	Y	N	Y	Y	N
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y	N	Y-	N	N	Y	N
Stability in Water	Y	N	Y		N	Y	N
Biodegradation	Y	N	Y	-	N	Y	N
Transport between Environmental Compartments	Y	N	-	Y	N	Y	N
(Fugacity)	Y			Y		Y	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	N	Y	-	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y			Y	Y	Y	N
Toxicity to Aquatic Plants	Y			Y -	Y	Y	N
TOXICOLOGICAL DATA							
Acute Toxicity	Y		Y	-	Y	Y	N
Repeated Dose Toxicity	Y		Y	-	Y	Y	N
Genetic Toxicity – Mutation	Y		Y	-	N	Y	N
Genetic Toxicity – Chromosomal Aberrations	Y		Y	-	N	Y	N
Developmental Toxicity	Y		Y	-	Y	Y	N
Toxicity to Reproduction	Y		Y	-	Y	Y	N

TEST PLAN DESCRIPTION FOR EACH SIDS ENDPOINT

A. Physicochemical

Melting point - A value for this endpoint was obtained from a reputable journal. .

Boiling Point - A value for this endpoint was obtained from a reputable journal.

Vapor Pressure - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN (1) and through the use of surrogate data.

Partition Coefficient - A value for this endpoint was obtained from a reputable journal..

Water Solubility - A value for this endpoint was obtained from a reputable journal.

Conclusion: All end points have been satisfied by utilizing data obtained from reputable journals and, where necessary, various physical chemical data modeling programs within EPIWIN or using measured values. The results of the various computer estimation models within EPIWIN have been noted by the Agency as acceptable in lieu of actual data or values identified from textbooks. No new testing is required.

B. Environmental Fate

Photodegradation - A value for this endpoint was obtained from a reputable journal.

Stability in Water - A value for this endpoint was obtained from a reputable journal.

Biodegradation - A value for this endpoint was obtained from a reputable journal.

Fugacity - A value for this endpoint was obtained from a reputable journal and the EQC Level III partitioning computer estimation model within EPIWIN.

Conclusion: All endpoints have been filled with data utilizing acceptable methodologies and of sufficient quality to fulfill these endpoints. No new studies are being proposed.

C. Ecotoxicity Data

Acute Toxicity to Fish - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.

Acute Toxicity to Aquatic Invertebrates - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.

Toxicity to Aquatic A value for this endpoint was obtained using a computer estimation-modeling program

Bioaccumulation A value for this endpoint was obtained from a reputable study.

Conclusion: All endpoints have been satisfied with data

D. Toxicological Data

Acute Toxicity - A value for this endpoint was obtained from a reputable journal.

Repeat Dose Toxicity - A value for this endpoint was obtained from a reputable journal.

Genetic Toxicity Mutation - A value for this endpoint was obtained from a reputable journal.

Aberration - A value for this endpoint was obtained from a reputable journal.

Developmental Toxicity - A value for this endpoint was obtained from a reputable journal.

Reproductive Toxicity - A value for this endpoint was obtained from a reputable journal.

Conclusion: All necessary endpoints have been satisfied with data on HCB

Common Name: 3,3' Dichlorobenzidine dihydrochloride

Structure:

Chemical Name: 3,3'-dichloro (1,1'-biphenyl) -
4,4'diamine; 3,3'-dichloro - 4,4' biphenyldiamine

Melting Point: 132-133 °C
Boiling Point: 402 °C
Acute Toxicity: LD50>3820 mg/kg,

SIDS DATA SUMMARY

Physical Chemical Endpoints
Data assessing the various physicochemical properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility) for DCB were obtained from experimental values reported in journals and reference works.

Environment
DCB breaks down rapidly in water that is exposed to natural sunlight and in air, but may last in soils for months. In air, half of the chemical is estimated to break down within two hours. In water exposed to natural sunlight, half the DCB is expected to break down in approximately 90 seconds. DCB is bioconcentrated by aquatic organisms under experimental conditions. In actual field study, DCB was not found in fish taken from waters in the vicinity of dye or textile manufacturing plants on the Buffalo and Delaware Rivers in the United States (Diachenko 1979).

Acute Toxicity

The acute oral LD50 values for rats are >3000 mg/kg bw for DCB.

Human Health

Laboratory animals exposed to moderate levels of DCB in the food for a long time suffered mild injury to the liver. In studies in which pregnant mice were exposed to the chemical, the kidneys of their offspring did not develop properly. Studies in laboratory animals indicate that DCB caused cancer of the liver, skin, breast, bladder, and tissues that form blood (leukemia) and other sites in animals that ate DCB in their food. There is no evidence that DCB has caused cancer in people who worked with it or who were exposed to it unknowingly or by accident for a short or long time. Due to the many types of cancer caused in different tissues of many different laboratory animals, DCB is thought of as a probable carcinogen.

Given that the pigment yellows manufactured using DCB are essentially not absorbed into the body, metabolism is not relevant. However, the presence of very low levels of 3,3'-dichlorobenzidine has been demonstrated in two studies using very sensitive techniques following oral administration of some yellow pigment compounds. It seems likely that this is due to the presence of a mono-azo impurity in some of the yellow pigment parent compounds, which is absorbed and subsequently metabolized. No DCB was found in the urine of experimental animals after exposure orally or via the lungs in long term studies. Following ingestion, the vast majority of the pigments are excreted unchanged in the feces.

Following ingestion, the vast majority of the pigments are excreted unchanged in the feces.

Conclusion

All endpoints have been satisfied with data, on DCB or through the use of estimations, which are of sufficient quality to conclude that no additional testing is needed.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the general US EPA guidance (3) and the systematic approach described by Klimisch *et al.* (4). These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. This scoring system was only applied to ecotoxicology and human health endpoint studies per EPA recommendation (5). The codification described by Klimisch specifies four categories of reliability for describing data adequacy. These are:

1. Reliable without Restriction: Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.

2. Reliable with Restrictions: Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.

3. Not Reliable: Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.

4. Not Assignable: Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

REFERENCES

1. EPIWIN, Version 3.10, Syracuse Research Corporation, Syracuse, New York.

2. US EPA. (1999). The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program. OPPT, EPA.

3. USEPA (1998). 3.4 Guidance for Meeting the SIDS Requirements (The SIDS Guide). Guidance for the HPV Challenge Program. Dated 11/2/98.

4. Klimisch, H.-J., Andreae, M., and Tillmann, U. (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. *Regul. Toxicol. Pharmacol.* 25:1-5.

5. USEPA. 1999. Determining the Adequacy of Existing Data. Guidance for the HPV Challenge Program. Draft dated 2/10/99.

I. General Information

CAS Number: Free 3,3' Dichlorobenzidine (CAS NO.: 91-94-1)

Name:

II. Physical-Chemical Data

A1. Melting Point

Test Substance

Test substance: DCB

Remarks:

Method

Method: Measured

Remarks:

Results

Melting point value: 132 °C

Remarks:

References

Merck. 1989. The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals. 11th ed.Rahway, NJ: Merck and Company, Inc., 482.

Other

Data is from a reputable reference.

B. Boiling Point

Test Substance

Test substance: DCB

Remarks:

Method

Method:

Remarks:

Results

Boiling point value: 402 °C

Remarks:

References

Hazardous Substance Data Bank, 1996, National Library of Medicine, National Toxicology Information Program, Bethesda, MD. Cited by ATSDR

Other

Data reported from reputable sources

C1. Vapor Pressure

Test Substance

Test substance: DCB

Remarks:

Method

Method: Estimate
Remarks:

Results

Vapor pressure value: .45
Temperature:

Remarks:

References

MPBPWIN v 1.40 in EPIWIN v 3.10, Syracuse Research Corporation, Syracuse, New York

Other

D. Partition Coefficient

Test Substance

Test substance: DCB

Remarks:

Method

Method: actual analysis
Remarks:

Results

Value: 3.2
Remarks:

References

Log Kow partition coefficient reported by Mabey et al. Aquatic Fate process data for organic priority pollutants, EPA Study No. 440/4-81-014, See Also Fate of 3,3' Dichlorobenzidine in Aquatic Environments, EPA Study No. 600/3-78-068, and ATSDR Toxicological Profile DCB

Other

E. Water Solubility

Test Substance

Test substance: DCB

Remarks:

Method

Method: The Solubility of DCB.2HCL in aqueous buffers of pH 4.6-8.9 at 22 degrees centigrade was determined spectrophotometrically from a knowledge of the extinction coefficients of its UV absorption maxima. The UV spectra of these solutions were recorded, and the values derived from at least two separately weighed methanol solutions, and from 4 to 6 spectral determinations.

Remarks:

Results

Value: 2-4 %
Temperature: 22 °C
Description: Slightly Soluble
Remarks:

References

Sikka HC, Appleton HT, Banerjee S. 1978. Fate of 3,3'-dichlorobenzidine in aquatic environments, U.S. Environmental Protection Agency. EPA-600/3-78-068.

Other

Environmental Fate Endpoints

A. Photodegradation

Test Substance

Test substance: DCB

Remarks:

Method

Method:

Test type: Water\sunlight and artificial laboratory lighting

Remarks:

Results

Temperature:

Degradation Rate

5-30 minutes in laboratory lighting

: Half-life

Ozone reaction: 90 seconds in natural light

Remarks:

Conclusions

References

Sikka HC, Appleton HT, Banerjee S. 1978. Fate of 3,3'-dichlorobenzidine in aquatic environments, U.S. Environmental Protection Agency. EPA-600/3-78-068.

Other

B. Stability in Water

Test Substance

Test substance:	DCB
Remarks:	

Method

Method:	estimates based on surrogate substances
Test type:	
GLP:	
Remarks:	

Results

Half-life:	½ life 100 days
Percent hydrolyzed in 5 days (120 hs) at 50 °C :	Hydrolysis rate 0/Mole per hour (Mabey et al.)
Remarks:	Under the conditions of an anaerobic biodegradation test with a similar compound (biazoaryl pigment), no hydrolysis was observed within 56 days

Conclusions

Data Quality

Remarks:

References

Other

Callahan MA, Slimak, Gabel NW, et al. 1979. Water-related environmental fate of 129 priority pollutants. V. II. U.S. Environmental Protection Agency. EPA-440/4-79-029b. See also, Mabey WR, Smith JH, Pod RT, et al. 1982. Aquatic fate process data for organic priority pollutants. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency. EPA 440/4-81-014. PB87-169090.

C. Biodegradation

Test Substance

Test substance:	DCB
Remarks:	

Method

Method:	EPA Microbial Degradation
Test type:	Microbial degredation in surface waters and activated sludge
GLP:	
Year:	
Remarks:	Two separate studies one 28 days the other 30 days the second used C^{14} labeling, Degradation was negligible in both studies. The third study used activated sludge

Results

Results:	
Remarks:	negligible biodegradation observed in all three studies

Conclusions

Data Quality

Remarks:	Data is very well documented, readily available and of very high quality.

References

Other

Sikka HC, Appleton HT, Banerjee S. 1978. Fate of 3,3'-dichlorobenzidine in aquatic environments, U.S. Environmental Protection Agency. EPA-600/3-78-068.

D. Transport between Environmental Compartments (Fugacity)

Test Substance

Test substance: DCB

Remarks:

Method

Test type: Estimation

Model used: Level III Fugacity Model; EPIWIN:EQC from Syracuse Research Corporation

Remarks:

Results

Model data and results:

Distribution (%)	
Air	1.13×10^{-5}
Water	47.5
Soil	52.4
Sediment	.095

Remarks:

Conclusions

Since no experimental values were available the physical chemical values utilized in this model were default parameters from within EPIWIN.

References

Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.

Other

The Level III model incorporated into EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay *et al.* 1996; *Environ. Toxicol. Chem.* **15(9)**, 1618-1626 and 1627-1637.

V. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance

Test substance:	DCB
Remarks:	

Method

Method:	EPA Bioconcentration
Test type:	Static
GLP:	N/A
Year:	1978
Species/strain:	Bluegill
Analytical monitoring:	Exposure solutions,
Exposure period:	96-Hour and 120 -Hour
Remarks:	Fish were exposed to 2 nominal concentrations(.5 and 2 mg/L), Glass containers were stored away from any light source

Results

Nominal concentration:	
Measured concentration:	
Endpoint value:	
Biological observations:	
Statistical methods:	
Remarks:	Significant mortality observed, surviving fish were severly intoxicated and would have succembed if the study contiued beyond 120 hours

Conclusions

Test substance is toxic to fish

Data Quality

Reliability:

Remarks:

Sikka et al. (1978) reported a 48-hour LC100 value for bluegill sunfish (Lepomis macrochirus) of 2 mg/litre 50% mortality was observed following exposure to 3,3'-dichlorobenzidine at 0.5 mg/litre for 96-120 hours. Based on quantitative structure-activity relationships, 96-hour LC50 values for fathead minnow (Pimephales promelas), rainbow trout (Oncorhynchus mykiss), and golden orfe (Leuciscus idus melanotus) have been estimated to be, 3 mg/litre, and 1.5 mg/litre, respectively (Government of Canada, 1993).

References

Other

Data is very well documented, readily available and of very high quality.

Sikka HC, Appleton HT, Banerjee S. 1978. Fate of 3,3'-dichlorobenzidine in aquatic environments, U.S. Environmental Protection Agency. EPA-600/3-78-068., See also, Appleton et al. Accumulation , elimination, and metabolism of dichlorobenzidine in the bluegill sunfish, Environ. Sci. Technol. Vol. 14, pp.50-54 (1980)

B. Acute Toxicity to Aquatic InvertebratesTest Substance

Test substance:

Remarks: DCB

Method

Method:
Test type:
GLP:
Year: estimate
Species/strain: Static
Analytical monitoring:
Exposure period: Daphnid (*Daphnia magna*)
Remarks: Temperature, pH and dissolved oxygen
48 Hours

Results

Nominal concentration:
Measured concentration:
Endpoint value:
Reproduction
Biological observations: LC 50 6664.850 mg/L
Statistical methods:
Remarks:

Conclusions

Data Quality

Reliability:
Remarks:

References

Other

Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210. The Level III model incorporated into EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay *et al.* 1996; *Environ. Toxicol. Chem.* **15(9)**, 1618-1626 and 1627-1637.

Due to characteristics in water and light, there are very few data on the acute toxicity of 3,3'-dichlorobenzidine to aquatic organisms. An IC50 of 0.06 mg/litre was reported for bacteria in the Microtox assay (Dutka & Kwan, 1981). ;

B2. Chronic Toxicity to Aquatic InvertebratesTest

Substance

Test substance:

Remarks: DCB

Method

Method:
Test type:
GLP:
Year: estimation
Species/strain:
Analytical monitoring:
Exposure period:
Remarks: Daphnid

16 days

Results

Nominal concentration:
Measured concentration:
Endpoint value:
Reproduction
Biological observations:
Statistical methods: EC 50 - 173.496 mg/L
Remarks:

Conclusions

Data Quality

Reliability:
Remarks:

References

Other

Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.

C. **Toxicity to Aquatic Plants**

Test Substance

Test substance:	DCB
Remarks:	

Method

Method:	Estimation
Test type:	
GLP:	
Year:	
Species/strain:	Green Algae
Endpoint basis:	
Exposure period:	96 Hours
Analytical procedures:	
Remarks:	

Results

Nominal concentration:	
Measured concentration:	
Endpoint value:	EC_{50} 3811.012 mg/L ChV 155.593 mg/L
NOEC:	
Biological observations:	
Was control response :satisfactory	
Statistical Methods:	ANOVA
Remarks:	

Conclusions

Data Quality

Reliability:	
Remarks:	

References

Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.

Other

V. Toxicological Data

A. Acute Toxicity

Test Substance

Test substance:	DCB
Remarks:	Purity was unknown

Method

Method:	Acute lethality; Other
Test type:	LD_{50} estimate
GLP:	No (Pre-GLP)
Year:	1974
Species/strain:	Rat/unknown
Route of exposure:	Oral gavage
Dose levels:	Unknown
Remarks:	

Results

Value:	LD_{50} = > 7070/3820 mg/kg.
Deaths at each dose:	
Remarks:	

Conclusions

Data Quality

Reliability:	Reliable with restrictions
Remarks:	The study was conducted quite some time ago and hence many study details are missing from the report and not available. However, basic data are given and results are consistent with other data for pigments of this class.

References

Gerarde HW, Gerarde DF. 1974. Industrial experience with 3,3'-dichlorobenzidine: An epidemiological study of a chemical manufacturing plant. J Occup Med 16(5):322-344.

Other

Repeated Dose Toxicity Test

Substance

Test substance:	DCB
Remarks:	

Method

Method:	repeated dose
Test type:	Sub acute
GLP:	no
Year:	1979
Species/strain:	Mouse Female
Route of exposure:	Ingestion
Duration of test:	6 or 12 months
Exposure levels:	54, 157, 4
Sex:	female
Exposure period:	6 an 12 months
Post-exposure observation period:	
Remarks:	

Results

NOAEL (NOEL):	<54mg/m3 Mortality: none Hepatomas in 8/8 at 6 months and in18/18 at 12 months

Conclusions Test substance may be considered toxic

Data Quality

Reliability:	Reliable without restriction
Remarks:	

References:

Osanai H. 1976. [An experimental study on hepatoma caused by aromatic amines.] Rodo Kagaku 52: 179-201. (Japanese)

Other

Repeated Dose Toxicity Test

Substance

Test substance:	DCB
Remarks:	

Method

Method:	repeated dose
Test type:	Chronic
GLP:	no
Year:	1978
Species/strain:	Dog, Beagle
Route of exposure:	Gavage
Duration of test:	6 weeks and 7.1 years
Exposure levels:	
Sex:	Male and female
Exposure period:	
Post-exposure observation period:	
Remarks:	

Results

LOAEL:	10.4 mg/kg/day heptacellular carcinomas in 4/6 papillary transitional cell carcinomas of urinary bladder in 5/6

Conclusions

Data Quality

Reliability:	Reliable without restriction
Remarks:	

References:

Stula EF, Barnes JR, Sherman H, et al. 1978. Liver and urinary bladder tumors in dogs from 3,3'-dichlorobenzidine. J Environ Pathol Toxicol 1(4):475-490.

Other

C. **Genetic Toxicity - Mutation**

Test Substance

Test substances:	DCB
Remarks:	

Method

Method:	In Vitro Mutagenicity
Test type:	Ames
GLP:	Unknown
Year:	1986
Species/strain:	Hamster liver / Salmonella typhimurium
Metabolic activation:	Yes, S9
Concentration tested:	
Remarks:	

Results

Result:	Positive
Cytotoxic concentration:	
Precipitation concentration:	Negative
Genotoxic effects	Negative
With activation:	
Without activation:	
Statistical methods:	
Remarks:	

Conclusions

Data Quality

Reliability:	Published study reliable without restriction
Remarks:	

References

Savard, S. and Josephy, PD. Synthesis and Mutagenicity of 3,3' Dihalogenated Benzidines, Carcinogenesis, Vol.7 pp.1239-1241, (1986) (cited in ATSDR)

D. Genetic Toxicity – Chromosomal Aberrations

Test Substance

Test substance:	DCB
Remarks:	Chromosomal aberation test CHO cells

Method

	no
Method:	
Test type:	Mouse Bone Marrow (Male and Female) Mouse Fetal Liver
GLP:	
Year:	1987
Species/strain:	
Exposure period:	
Remarks:	

Results

Result:	Negative femal bone marrow, positive male bone marrow and fetal liver
Genotoxic effects:	
Concentration tested	
Statistical methods:	
Remarks:	

Conclusions

Data Quality

Reliability:	Reliable without restriction
Remarks:	

References

Cihak R., Vontorvoka M. "Benzidine and 3,3' Dichlorobenzidine Induce Micronuclei inthe Bone Marrow and the FetalLiver of Mice after Gavage", Mtugenesis Vol.2 pp. 267-269 (1987) See also

Other

Iba MM, Ghosal A, Poyer JL, et al. 1991. In vivo spin-trapping of the radical metabolites of 3,3,'dichlorobenzidine and related compounds in the rat. Progress in Pharmacology and Clinical Pharmacology 8(3):255-266.
Ashby J, Mohammed R. 1988. UDS activity in the rat liver of the human carcinogens benzidine and 4-aminobiphenyl and the rodent carcinogens 3,3'-dichlorobenzidine and Direct Black 38. Mutagenesis 3(1):69-7 1.

E. Developmental Toxicity

Test Substance

Test substance: DCB

Remarks:

Method

Method:

GLP: See Repeated Dose Studies

Year:

Species/strain:

Sex:

Route of exposure:

Exposure levels:

Actual doses received:

Exposure period:

Duration of test:

Remarks:

Results

Maternal toxicity

NOEL:

NOEL for teratogenicity:

NOEL for fetotoxicity:

Parental toxic responses:

Fetal toxic responses dose:

Statistical Methods:

Remarks: Studies in which pregnant mice were exposed to the chemical, the kidneys of their babies did not develop properly.

Conclusions

Data Quality

Reliability:

Remarks: Golub et al. Oncogenic Action of Some Nitrogen Compounds on the Progeny of Experimental Mice" Bull. Exp. Biol. Med. Vol.78 pp. 1402-1404 (1975) (Russian)

References

Other

F. Toxicity to Reproduction

Test Substance

Test substance: DCB
Remarks:

Method

Method:
GLP:
Year:
Species/strain:
Sex:
Route of exposure:
Exposure levels:

Exposure period:

Duration of test:
Remarks:

Results

Maternal toxicity NOEL:
Parental toxic responses:
Fetal toxic responses dose:
Statistical Methods:
Remarks:

Conclusions

Data Quality

Reliability:
Remarks:

References

Other

Acute toxicity

Test substance: DCB

Remarks:

Method

Method:	Irritation to the rabbit eye
Test type:	eye irritation
GLP:	yes
Year:	1974
Species/strain:	rabbit, New Zealand albino (chbb:Nzw)
Route of exposure:	
Dose levels:	
Remarks:	

Results

Value:	Cornea .55, iris .33 conjunctive (redness) 2.44) (Chemosis .88)
Deaths at each dose:	
Remarks:	observation times Reversibility within

Conclusions NOAEL 100 mg

Data Quality

Reliability:	reliable without restriction
Remarks:	

References Gerarde HW, Gerarde DF. 1974. Industrial experience with 3,3'-dichlorobenzidine: An epidemiological study of a chemical manufacturing plant. J Occup Med 16(5):322-344.

Other

Acute toxicity

Test substance:	DCB
Remarks:	

Method

Method:	Skin irritation to the rabbit
Test type:	Skin irritation intradermal installation SEMIOCCLUSIVE
GLP:	N/A
Year:	1974
Species/strain:	rabbit New Zealand albino
Route of exposure:	
Dose levels:	700 mg/kg
Remarks:	

Results

Value:	not irritating
Deaths at each dose:	
Remarks:	

Conclusions not irritating

Data Quality

Reliability:	Valid without restriction
Remarks:	

Reference

Gerarde HW, Gerarde DF. 1974. Industrial experience with 3,3'-dichlorobenzidine: An epidemiological study of a chemical manufacturing plant. J Occup Med 16(5):322-344.

Chronic Dose Toxicity Test Substance

Test substance:	DCB

Method

Method:	Chronic Toxicity
Test type:	Repeated oral dose
GLP:	unknown
Year:	See references below
Species/strain:	Rat,dogs, hamsters,mice
Route of exposure:	Oral gavage
Duration of test:	104 Weeks
Exposure levels:	1 to 7 years
Sex:	Male and Female
Exposure period:	
Post-exposure observation period:	
Remarks:	

Results

NOAEL (NOEL):	Vary by study

Conclusions Neoplasia in a variety of target organs and a variety of species

Data Quality

Reliability:	published data, valid without restriction
Remarks:	

References

blastomogenic agent] Vop Onkol 5(5):524-533.
experimental study on hepatoma caused by aromatic
(Japanese) Sellakumar AR, Montesano R,
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